REMARKS/ARGUMENTS

Claims 22-35 were pending in this application. According to the May 21, 2003 final Office Action, claims 22-35 were rejected. Applicant has canceled claim 26 and amended claim 22. Accordingly, claims 22-25 and 27-35 are under consideration. Applicant maintains that the amendments do not introduce any new matter. Specifically, support for the amendments in claim 22 may be found in the specification on page 5, lines 18-21 and on page 7, lines 3-5.

Rejection under 35 U.S.C. §112

The Examiner maintained his rejection of claims 22-35under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the claimed invention.

In response, Applicant respectfully traverses the Examiner's rejection. Applicant maintains that the present invention as taught in the specification can be used with plant species other than tobacco and leads to the desired success.

The present invention provides a process by which the amount of reserve material of plant seeds can be modified in a specific way. This is achieved by the reduction or elimination of the expression of that endogenous invertase inhibitor protein which is predominantly expressed in ovules of a plant during the seed development. The reduction or elimination of the expression of the invertase inhibitor results in an increase of the activity of that invertase which is regulated by the invertase inhibitor during the seed development. The increased activity of the invertase then leads to an increased accumulation of reserve material in the seeds. The reduction or elimination of the expression of the invertase inhibitor is affected by an anti-sense inhibition by using a nucleotide sequence encoding the invertase inhibitor, whereby the nucleotide sequence exactly corresponds to that nucleotide sequence whose transcription and/or translation in the plant shall be reduced or eliminated.

According to the claim 22, as amended, the nucleotide sequence used must fulfill two requirements:

1) The nucleotide sequence encodes that invertase inhibitor which is expressed during the seed development. This means that the nucleotide sequence encodes that invertase inhibitor expressed in young ovules.

2) The nucleotide sequences are obtained from exactly that plant species in which the nucleotide sequence shall be introduced.

Both the example described in the application (tobacco plant) and the example described in the previously submitted Declaration (rape plant) prove that the present process results in transgenic plants whose seeds have a modified, that is increased amount of reserve material. Rape and tobacco are plant species which are not closely related to each other and belong to different plant families. Both examples prove that the process of the present application can be used with different plant species and different plant families. Both examples therefore prove that the process of the present application can be used with plant species other than tobacco and rape.

The goal of the present invention is not to provide a plurality of different genes encoding the invertase inhibitor from a plurality of plant species nor is it to develop new procedures for the isolation of such sequences. As outlined above, the present invention provides processes for modifying the amount of reserve material of seeds whereby of course known sequences and known procedures can be used. Tobacco was merely selected as an example to show that the present process is practicable.

The present teaching contains clear instructions how to proceed in order to modify or increase the amount of reserve material in seeds of a plant. From the wording of claim 22 it is clear which nucleotide sequence should be used. Furthermore, in the application several suitable

procedures are described how such nucleotide sequences can be isolated with a reasonable chance of succeeding.

However, it is noteworthy that the present application is directed to the competent person skilled in the art. The person skilled in the art is an artisan in that field in which the application lies. That is, this artisan has special knowledge in the field of plant molecular biology. This artisan has access to all relevant documents and information of his special field. This artisan knows that various sequences encoding invertase inhibitors in different plant species have already been isolated and identified. This artisan knows which of these sequences can be used in the present process. This artisan also has the knowledge to identify and to isolate suitable nucleotide sequences from plant species from which such nucleotide sequences are so far not known.

Therefore, Applicant maintains that it is not necessary to list all suitable known nucleotide sequences and all possible or conceivable embodiments in the application.

The document of Broun et al., PNAS, 98 (2001), 8925-8927, is not relevant

The document of Broun is also not relevant for factual reasons. Broun describes that the overexpression of rate-limiting enzymes may not result in enhanced flux through the pathway. Overexpression occurs if the copy number of the gene encoding the enzyme will be increased or if regulator mechanisms which normally limit the transcription/translation of the gene (and thus the expression of the gene product) will be changed in such a way, that the amount of the enzyme synthesized is increased in comparison to the normal state. Therefore, an overexpression always results in an increase of the amount of the gene product (i.e., the enzyme) expressed in comparison to the normal state. This leads to an increased activity of the gene product, which is higher than the maximum activity reached under normal circumstances.

However, the situation concerning the present invention is completely different. Here, a nucleic acid encoding the inhibitor is introduced in anti-sense orientation into a plant. By this the

expression of the inhibitor protein will be reduced or eliminated. That is, the amount of the inhibitor protein will be reduced or eliminated in comparison to the normal state. Since the invertase inhibitor regulates the activity of the invertase via protein-protein interactions in a development-specific manner, a reduced amount of inhibitor protein results in an increase of the invertase activity (during a specific developmental phase). However, the amount of the invertase itself is not increased. Thereby the maximum activity of the invertase, reached during certain developmental phases, will never be exceeded.

Objection that the anti-sense effect in stamens might indicate to unforeseen mechanisms of regulation

On page 11, line 35 to page 12, line 2 of the specification, it is stated that in the ovary of anti-sense transformants the amount of invertase inhibitor is sharply decreased whereas in stamens only a slightly modified inhibitor expression can be seen, presumably because several inhibitor isoforms are expressed in this tissue.

Applicant would like to make the following points t reply to the Examiner's assertion that this would indicate to unforeseen mechanisms of regulations and that an unpredictability of this kind would require undue experimentation in attempts to increase the amount of reserve material in seeds:

1) As outlined in the description, the anti-sense inhibition results in a strong reduction of the expression of the inhibitor protein in the ovary, i.e. exactly that organ from which seeds develop.

2) Stamens do not play any role during seed development. Therefore, it is not relevant whether the expression of the inhibitor protein in stamens is reduced or not.

3) The use of the present procedure resulted both in case of tobacco and rape in an increase of the amount of reserve material in seeds. This shows that the expression of the

inhibitor protein in stamens is completely irrelevant. It furthermore shows the extremely high specificity of the present procedure, namely that only the expression of the inhibitor protein within the ovary is reduced, but not in other tissues of the plant or the flower.

4) On page 12, last paragraph, of the specification it is stated, that the entire vegetative development phase of the inhibitor anti-sense transformants proceeds without a visible phenotype. On page 12, second paragraph, of the specification it is furthermore stated that the modified activity of the cell wall invertase during the seed development does not affect the dry weight/seed, the stored oil content/seed and the total protein content/seed, but not the total number of seeds/flowers, and also not the seed size. This also shows the high specificity of the present procedure, namely that only the development of the ovary is modified.

5) The high specificity of the present procedure is based on the use of a nucleotide sequence which encodes that inhibitor which is expressed during the seed development within the ovary and whose expression shall be reduced.

In summary, this shows that by practicing the present procedure one is not faced with unforeseen mechanisms of regulations and that there is no unpredictabiltiy. The present teaching does not require undue experimentation.

Objection concerning the use of sense constructs

Since the present examples do not show that sense constructs result into plant seeds with an increased amount of reserve material, Applicant has amended claim 22 to delete the use of sense constructs. Also, claim 26 has been deleted.

Objection concerning the use of probe sequences which do not show a 100% homology

The isolation of gene sequences via the isolation of proteins and subsequent determination of the amino acid sequence is a routine measure known for a long time. As the person skilled in the art appreciates, this approach has been successfully used for the isolation of

numerous genes. Without this approach, only a minor fraction of all those genes known would have been isolated. The fact that primers that do not show 100% homology may have to be used has no influence on the fact, that by this approach desired sequences can be isolated with a reasonable expectation of success.

The possibility, that by using primer sequences with less than 100% homology, gene sequences other than the desired gene sequences are isolated, can for example be decreased by the use of tissues as starting material which are enriched concerning the sequences to be isolated (for example flowers with young ovules as indicated by amended claim 22). The young ovule comprising the ovary is the largest organ within the flower. Furthermore, the inhibitor protein which is to be inhibited according to the application is predominantly expressed in the young ovule. Also, the homology of the nucleotide sequences encoding the inhibitor protein to be inhibited to other nucleotide sequences encoding different proteins is relatively low. This means that the chance to isolate a nucleic acid other than the desired nucleic acid is therefore low and negligible.

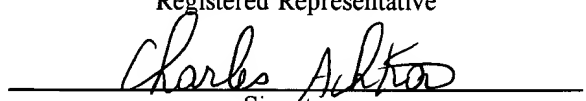
In summary, the present invention as taught in the specification is based on procedures for isolating sequences which are known and which have proven their utility. Therefore, applicant maintains that the present invention as taught in the specification can be used with plant species other than tobacco and leads to the desired success. Accordingly, the Examiner is kindly requested to withdraw this rejection.

In light of the foregoing, it is respectfully submitted that this application is now in condition to be allowed and the early issuance of a Notice of Allowance is respectfully solicited.

If there are any issues or amendments the Examiner wishes to discuss, the Examiner is encouraged to contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on July 30, 2003:

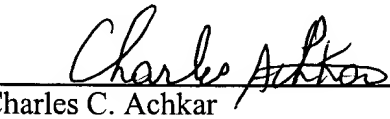
Charles C. Achkar
Name of applicant, assignee or Registered Representative



Signature

July 30, 2003
Date of Signature

Respectfully submitted,



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